Claims

1. A modified extracellular domain of a cytokine receptor protein, capable of being crystallized without being complexed to a ligand molecule.

2. A modified protein according to claim 1 being a homo- or heterodimeric cytokine receptor.

3. A modified protein according to ~~claims 1 or 2~~ claim 1 wherein at least one molecule segment which contributes to a disordered structure is deleted.

4. A modified protein according to claim 3 truncated in at least one terminal end.

5. A modified protein according to claim 4 truncated in its C-terminal end and in its N-terminal end.

6. A modified protein according to claim 5 being human growth hormone receptor (hGHR).

7. A modified human growth hormone receptor (hGHR) according to claim 6 having 31 or 33 amino acid residues removed in its N-terminal end.

8. A modified human growth hormone receptor (hGHR) according to claim 6 ~~or 7~~ having 3 or 4 amino acid residues removed in its C-terminal end.

9. A modified human growth hormone receptor (hGHR) according to any of claims 6 to 8 consisting of residues 32-237, 32-234 or 34-233 of the native molecule.

10. A modified human growth hormone receptor (hGHR) according to claim 9 consisting residues 32-237 of the native molecule.

11. Crystals of a receptor protein according to any of claims 1 to 10 to any of claims 1-10 suitable for binding studies with ligand candidates.

12. Crystals according to claim 11, wherein the contact surface between two molecules is between 200 to 1800 $Å^2$ (square ångström) and more preferably between 100 to 900 $Å^2$ (square ångström).

13. Crystals according to claim 11 ~~or 12~~ containing at least 50 % (v/v) of a solvent acceptable for binding studies.

14. Crystals according to claim 13 containing about 60 to 80 % (v/v) of a solvent.

15. Crystals according to any of claims 11 to 14 capable of being frozen with gaseous or liquid nitrogen with maintained capacity of diffraction to at least 3.5 Å by using synchrotron radiation source.

16. Crystals according to claim 15 capable of being frozen with gaseous or liquid nitrogen with maintained capacity of diffraction to at least 3.5 Å by using synchrotron radiation source.

17. Crystals according to any of claims 11 to 16 capable of being resistant to an addition of up to 10% (v/v) of DMSO (dimethylsulfoxide) and up to 5 % (v/v) of DMF (dimethylfluoride) for at least 24 hours.

18. Crystals according to any of claims 11 to 17 **characterized in that** they are formed at pH between 5.0 to 8.5.

19. Crystals according to claim 18 **characterized in that** they are formed at a pH between 7.0 and 8.0.

20. Crystals according to any of claims 11 to 17 formed in the presence of one or more salts having a concentration between 0.15 M and 1.0 M.

21. Crystals according to claim 20, wherein the salt(s) is(are) selected from a group consisting of ammonium sulfate, lithium sulfate, sodium phosphate, potassium phosphate, sodium chloride, lithium chloride, ammonium acetate, sodium acetate, magnesium chloride, sodium formate and sodium citrate.

22. A method of designing drugs with cytokine receptor activity by employing the crystals according to ~~any of claims 11 to 21~~ claim 11 in binding studies with selected ligand candidates.

23. A method according to claim 22 involving dimerization of the receptor.

24. A method according to claims 22 or 23, wherein the crystals are soaked or co-crystallized with a solution comprising the ligands.

25. A method according to any claims 22 to 24, wherein the receptor is a modified growth hormone receptor investigated with ligands having potential growth hormone activity.

26. A method of obtaining improved cytokine receptor crystals involving the ~~subsequent~~ steps of:

(i) solving the receptor three-dimensional structure complexed to a ligand by crystallographic methods,

(ii) identifying regions of the receptor molecule which may contribute to disorder in a crystalline state,

(iii) producing modified receptor molecules without said regions, and

(iv) crystallizing the modified receptor without the presence of a ligand.

27. A method according to claim 26 involving the extracellular part of the receptor.

28. A method according to claim 26 ~~or 27~~, wherein said receptor is human growth hormone receptor.

29. A method according to claim 28, wherein said ligand is human growth hormone.

Add C1 Add S2

Add A1e